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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,631	01/28/2004	Zhong Zhang	TPIP018X2	3752

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EXAMINER	
GEMBEH, SHIRLEY V	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 10/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/766,631	ZHANG ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,11,12,20,23-37,39-64 and 71-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,11,12,20,23-37,39-64 and 71-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The response filed July 12, 2006 presents remarks and arguments. Claims 1, 11-12, 20, 23-37, 39-64 and 71-78 are pending in the application. Applicant request for reconsideration of the rejection of claims in the last office action has been considered.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/05/06 has been entered.

Status of claims

Claims 1, 11-12, 20, 23-37, 39-64 and 71-78 pending.

Claims13-19, 21, 23, 65 and 70 are cancelled.

Claims 1, 11-12, 20, 23-69 and 71-75 are amended.

Claims 75-78 are newly added.

Response to Arguments

Applicants' arguments, filed July 12, 2006, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant should submit an argument under the heading "Remarks" pointing out disagreements with the examiner's contentions. Applicant must also discuss the references applied against the claims, explaining how the claims avoid the references or distinguish from them.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 11-12, 20, 23-37, 49-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Applicant has not conveyed possession of the invention with reasonable clarity to one skilled in the art. In particular, Applicant has not provided a description of the structure of a representative number of derivative compounds nor a description of the chemical and/or physical characteristics of a representative number of compounds nor a description of how to obtain a representative number of specific compounds.

To satisfy the written description requirement, applicant must convey with reasonable clarity to one skilled in the art, as of the filing date that application was in possession of the claimed invention. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967). For example Claim 1 employing one or more pH modifiers, stabilizers or tonicity modifiers are not described nor exemplified and does not inform the public of the limits of the monopoly asserted.

II. Claims 1, 11-12, 20-37 and 39-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain new subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Nowhere in the specification is there a mention of "on a gram per ml w/v". The specification has no definition for weight/volume.

III. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-12, 23-26, 40-48, 50-55, 63-64, 66, 72 and 78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
The "term from about", "less than about", "about" "between about" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention, because one of skill will not be able to determine which term is in control.

IV. Claims 51-57 recites the limitation "poloxamer 188" in claim 50. There is insufficient antecedent basis for this limitation in the claim.

V. Claim 78 is rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that claim 78 fail(s) to correspond in scope with that which applicant(s) regard as the invention can be found in the listed claims 1, 49, 66, 71 and 75, where Applicant disclose a clear aqueous pharmaceutical composition. How can a clear aqueous pharmaceutical composition have a particle size from 30-75 nanometers? Unless the solution is semi-solid, then it is not transparent or clear to the eye.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 49-64, 66-68 and 71-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glen et al US 4,056,635 taken with Meadow et al., WO 03/017977 A1 in view of May et al., US 6,140,374 and Lee et al., US 6,743,436 B1.

Glen et al teach the instant claim 1 an aqueous formulation comprising:

a. 2,6-diisopropylphenol (see col. lines 22-23) b. water (see col. 3 lines 30), a block copolymer (see col.3 lines 26-27) polyethylene glycol (see col. 3 lines 29-30) a pH modifier citric acid (see col. 3, lines 7-10) and said solution is clear (see example 9). Claims 49-57 where the total amount of the block polymer is from 5-10% of said formulation (see col. 3 lines 27-28) an over lap of the range exist, therefore will be obvious to one of ordinary skill to modify to achieve the instantly claimed invention. Claims 13 where the block copolymer –is a poloxamer 188 (pluronic 68 see col. 3 lines 27-28). Poloxamers are block copolymer therefore meets the limitation in claim 49 and 50.

With regards to claim 16 and 20, Glen et al. also teaches the amount of 2,6-diisopropylphenol is 1% (see col. 3 line 65), in claims 51-57 the 2,6-diisopropylphenol is from 1-5% (see col. 3 line 62), and in claim 19, the 2,6-diisopropylphenol is 1-2 % is recited at (see col. 3 lines 62-66).

Claims 49-57, the PEG is 10 %(which is included in the range up to 15%), therefore the claim limitations are met (see col. 6 line 7-8). Glen teaches current claim 49, 58, 67 contains citric acid in the composition (see col. 9 lines 12-14).
Glen also teaches the formulation is administered to a mammal (see col.1 lines 5-7) to induce anesthesia recited in claim 73. Claim 74 is obvious, as the formulation will comprise a container because in other to dispense the formulation would have to be in a container.

As to claim 49, 66 and 72, Lee teaches the block copolymer is less that 10 % (see cols. 7 and 8). Lee et al. also teach an aqueous solution containing a poloxamer 188 in an amount of 8% (see col. 7 line 32+) in claims 51, 52, 56, and 7% as recited in claims 53-54 and 57 (see 6 line 65+). Also the reference teaches the range of PEG from 0.5-5% (see col.7 lines 16-65) as recited in claims 39-57. The lee reference also teaches the formulation contains polysorbate (see col. 7 lines 47-50) recited in claim 62. The polyoxyethylene 20 sorbitan is present in 2% (see col. 7 lines 47-50) in claim 63.

May et al. teach current claims 60-61, 66 and 68 a pharmaceutical formulation containing an antimicrobial agent –benzyl alcohol (see abstract). As to claim 49, 2,6-diisopropylphenol is recited as 1 and 2% w/v of said formulation (see col. 2 line 14) and 1% by w/v (see col. 2 line 16) as in claims 40-48, 51-55.

Although Glen et al. did not state the concentration of the citric acid as disclosed in the instant application, the use of citric aid is to maintain the pH of the composition, therefore one of ordinary skill in the art will modify the concentration of the acid to achieve the desired pH level of the formulation.

Also the combine above reference teaches a wide concentration range for copolymers, PEG, citric acid. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to formulate a sterile composition ranges replace the concentration as disclosed in the 635 patent with that of the applicant as the formulation contains all the necessary components for anesthesia in a patient. Although, Glen did not per se teach of the exact concentration of the components, Lee et al, however provided motivation to optimize the ranges of surfactants used with the lipid, based upon the examples given (see col. 6), where 4 grams of the surfactant and 0.5 g of PEG versus, 8 grams surfactant and 5 grams PEG, indicating concentration ranges can be optimized, based, upon the lipid use as soluble lipid-soluble drugs are generally poorly soluble in water and possesses limitation as disclosed by Lee et al. (col. 1 lines 64+). Lee further explained (see col. 5. line 4+), the effect of selecting a suitable surfactant to increase the surface tension.

One of ordinary skill in the ad would have been motivated to combine the teachings of Glen with that of Meadow et al. May et al. and Lee et al. which result in the concentrations as claimed and obtained successful results in administering the formulation as an anesthetic to patients. One of the ordinary skills in the art would have known administering anesthesia to patients would vary as to tolerance, and the

condition of the patient in need. It would have been obvious to one of ordinary skill in the ad to add an antimicrobial to the solution to prevent microbial growth in compositions intended for human and/or veterinary use. Therefore the skilled artisan would have incorporated an anti bacterial agent to the formulation.
One of ordinary skill in the art would have expected successful results and would have been motivated combining the teachings of the above cited references as the art recognizes the claimed formulation (claim 49) for use as an anesthesia.

Lastly, it would have been obvious to one of ordinary skill in the art to use a purified poloxamer, since the formulation is intended for human.

Thus, the claimed invention was prima facia obvious to make and use at the time it was made.

Claims 75-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glen et al US 4,056,635 in view of Meadow et al., WO 03/017977 A1 as applied to claims 49-64, 66-68 and 71-74 above, and further in view of May et al., US 6,140,374 and Lee et al., US 6,743,436 B1.

For the same reasons given above, the use of sodium or potassium hydroxide and hydrochloric acid are well known in the art for modifying pH. One of ordinary skill would have employed any of the pH modifiers to adjust the pH of the solution, use the base to titrate for pH ranges in the basic range or the hydrochloric acid to adjust in the acidic range.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SVG
10/14/06

Ardin H Marschel 10/15/06
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